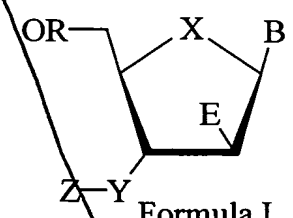
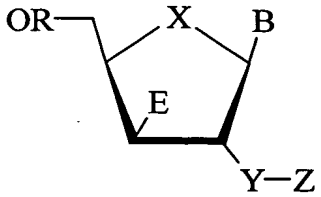
What is claimed is:

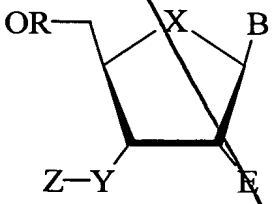
1. A method for the treatment of hepatitis B virus (HBV) infection comprising administering an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



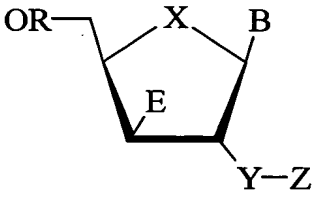
Formula I



Formula III



Formula II



Formula IV

wherein:

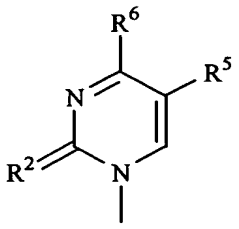
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

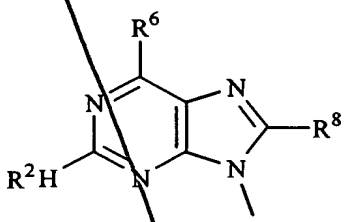
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



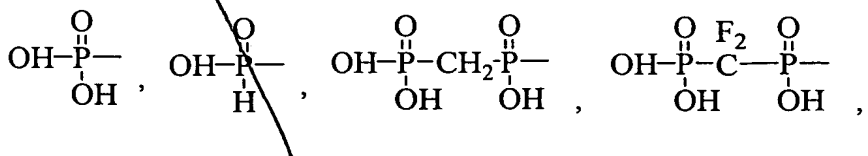


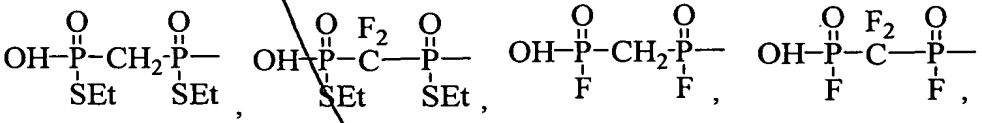
R^2 is selected from the group consisting of O, S, NH, NR;

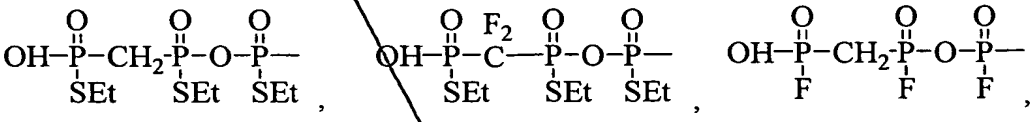
R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

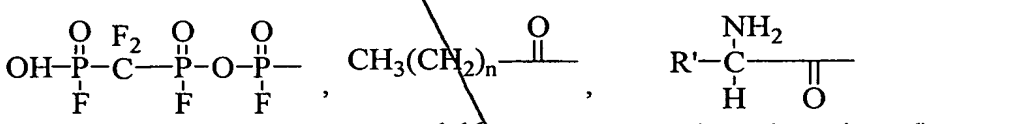
R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of









n=1-16

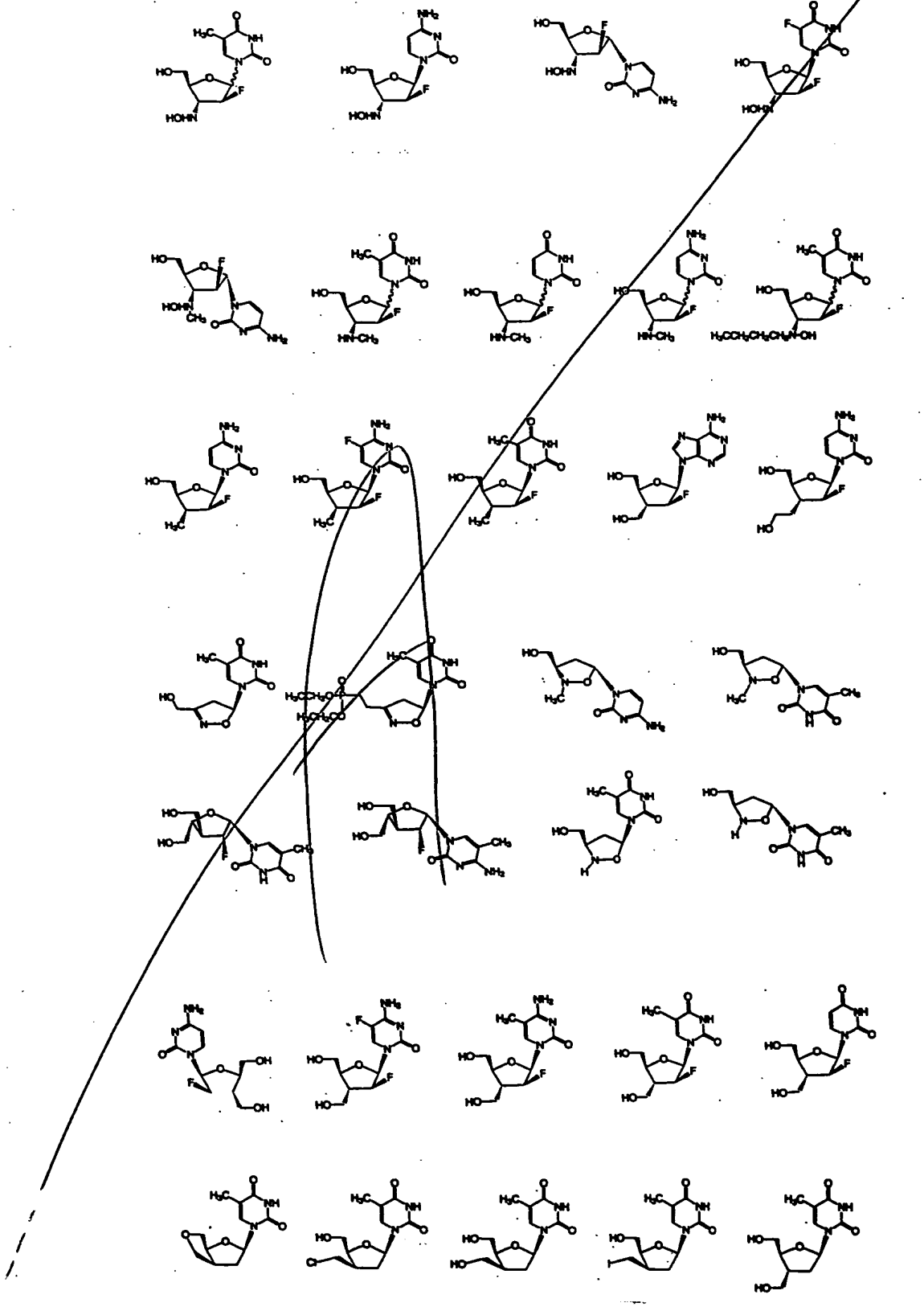
(D- and L-aminoacyl)

or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

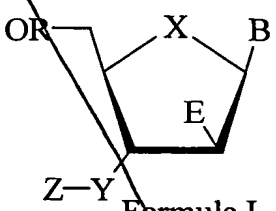
2. The method of Claim 1, further comprising administering the compound in combination or alternation with one or more additional anti-HBV agents.

3. The method of Claim 2, wherein the additional anti-HBV agent is selected from the group consisting of FTC (the (-)-enantiomer or the racemate), L-FMAU, interferon, beta-D-dioxolanyl-guanine (DXG), beta-D-dioxolanyl-2,6-diaminopurine (DAPD), beta-D-dioxolanyl-6-chloropurine (ACP), beta-D-dioxolanyl-2-aminopurine (ADP), famciclovir, penciclovir, bis-POM PMEA (adefovir dipivoxil); lobucavir, ganciclovir, ribavarin, lamivudine (3TC), L-thymidine (L-dT), L-2'-deoxycytidine (L-dT), L-2'-deoxycytidine-3',5'-di-O-valyl (D or L), entecavir (BMS-200475), adefovir, L-D4FC, D-D4FC, and mycophenolic acid (an IMPDH inhibitor).

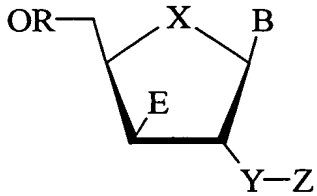
4. The method of Claim 1, wherein the compound is selected from the group consisting of



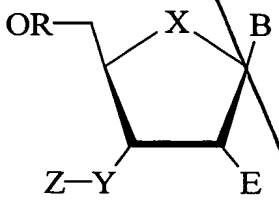
5. A method for the treatment of hepatitis C virus (HCV) infection comprising administering an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



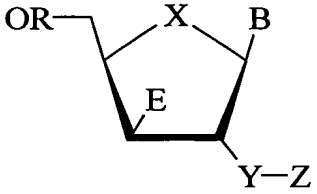
Formula I



Formula III



Formula II



Formula IV

wherein:

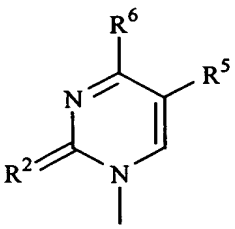
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

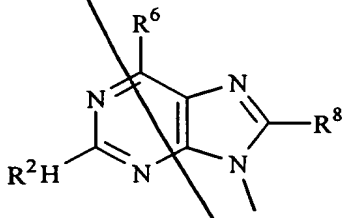
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



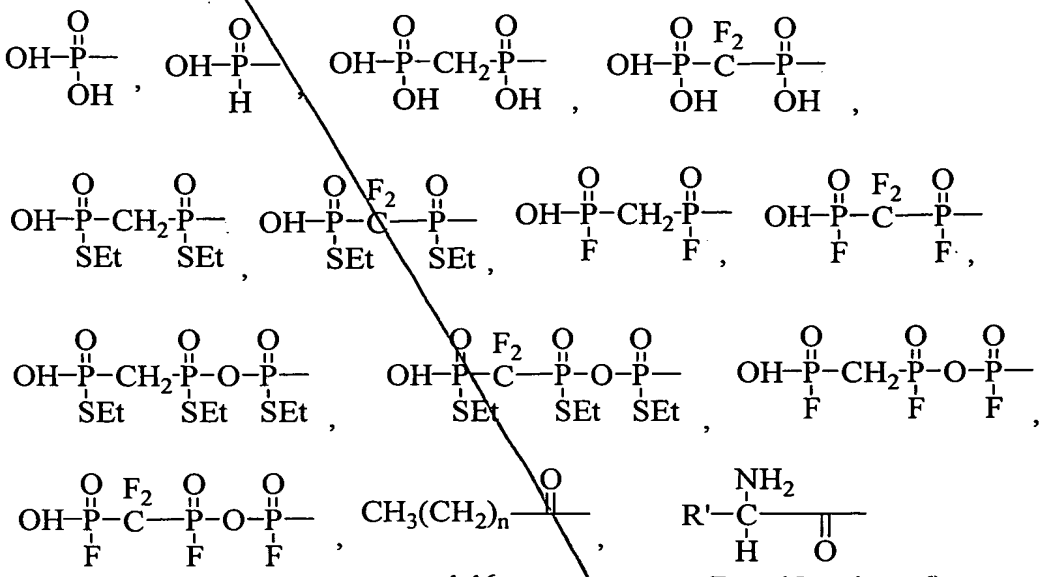


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH{=}CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of



n=1-16

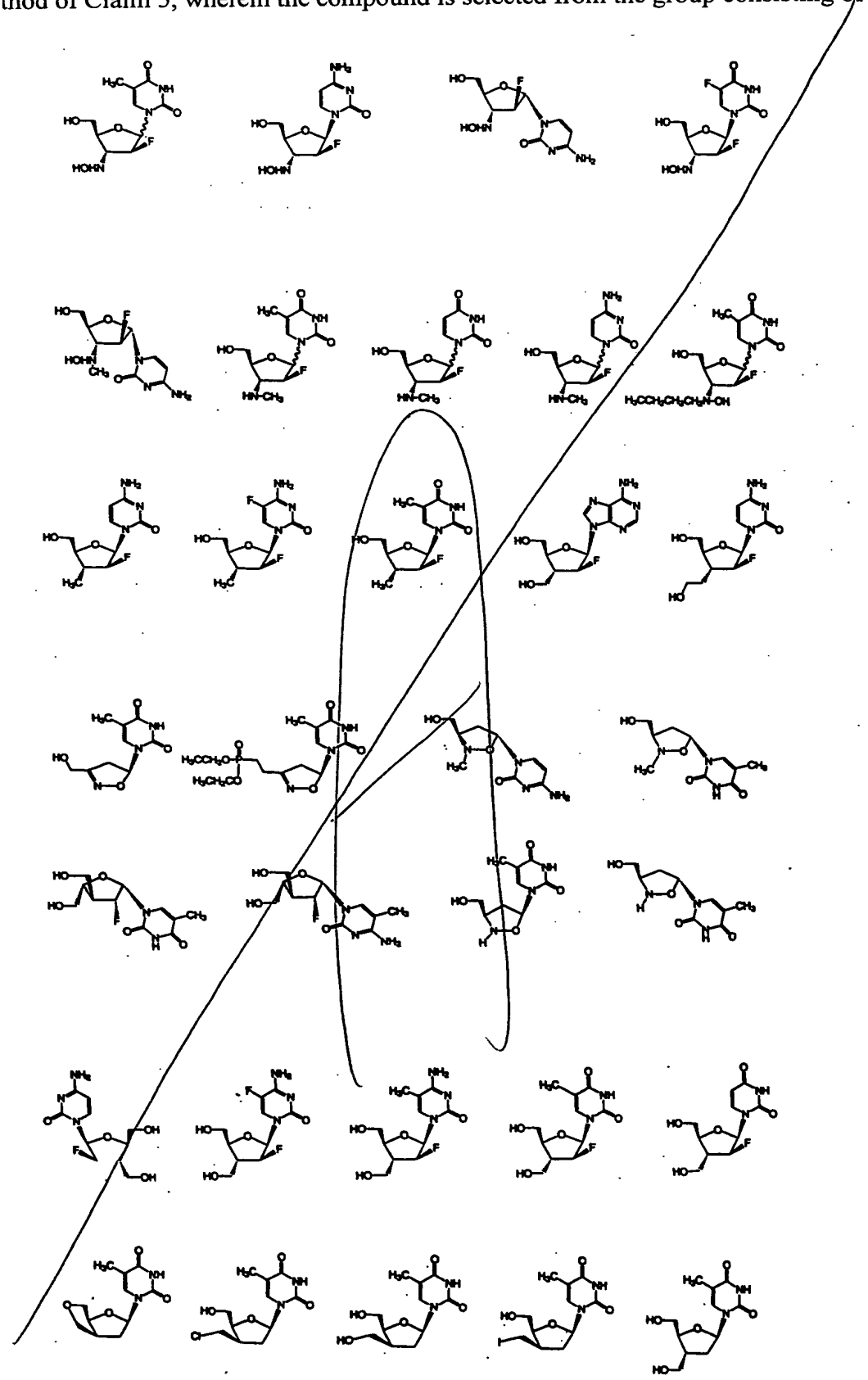
(D- and L-aminoacyl)

or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

6. The method of Claim 5, further comprising administering the compound in combination or alternation with one or more additional anti-HCV agents.

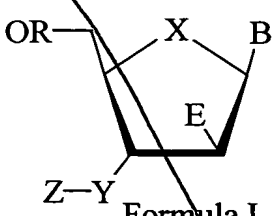
7. The method of Claim 6, wherein the additional HCV agent is selected from the group consisting of interferon, macrokine, heptazyme, ribavarin (D and L), amantadine, ofloxacin, zadaxin and reticulose.

8. The method of Claim 5, wherein the compound is selected from the group consisting of

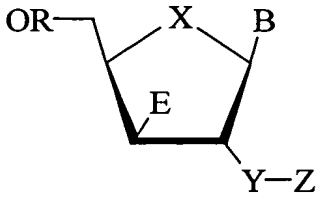


Sub A3

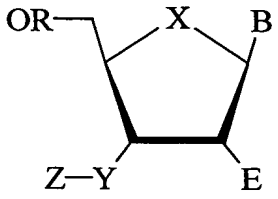
9. A method for the treatment of hepatitis D virus (HDV) infection comprising administering an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



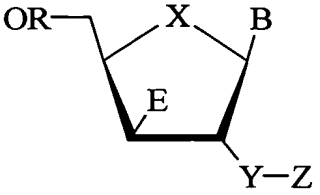
Formula I



Formula III



Formula II



Formula IV

wherein:

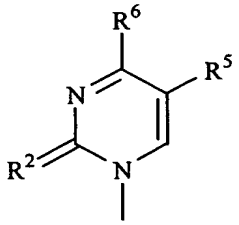
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

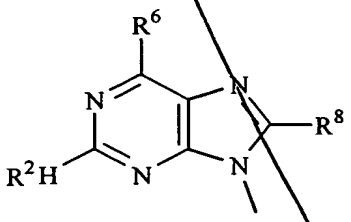
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



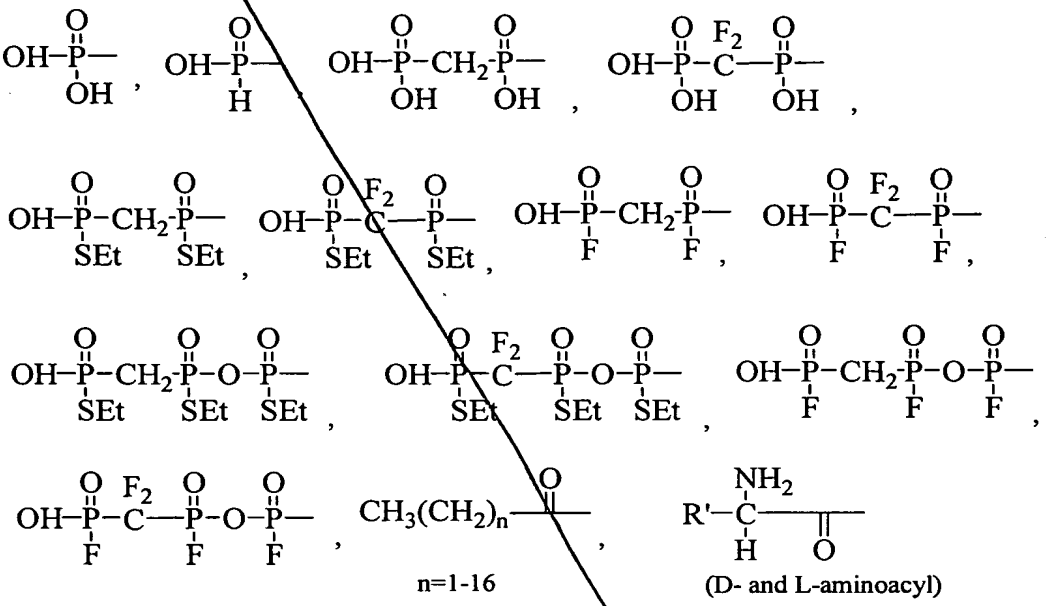


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH{=}CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of

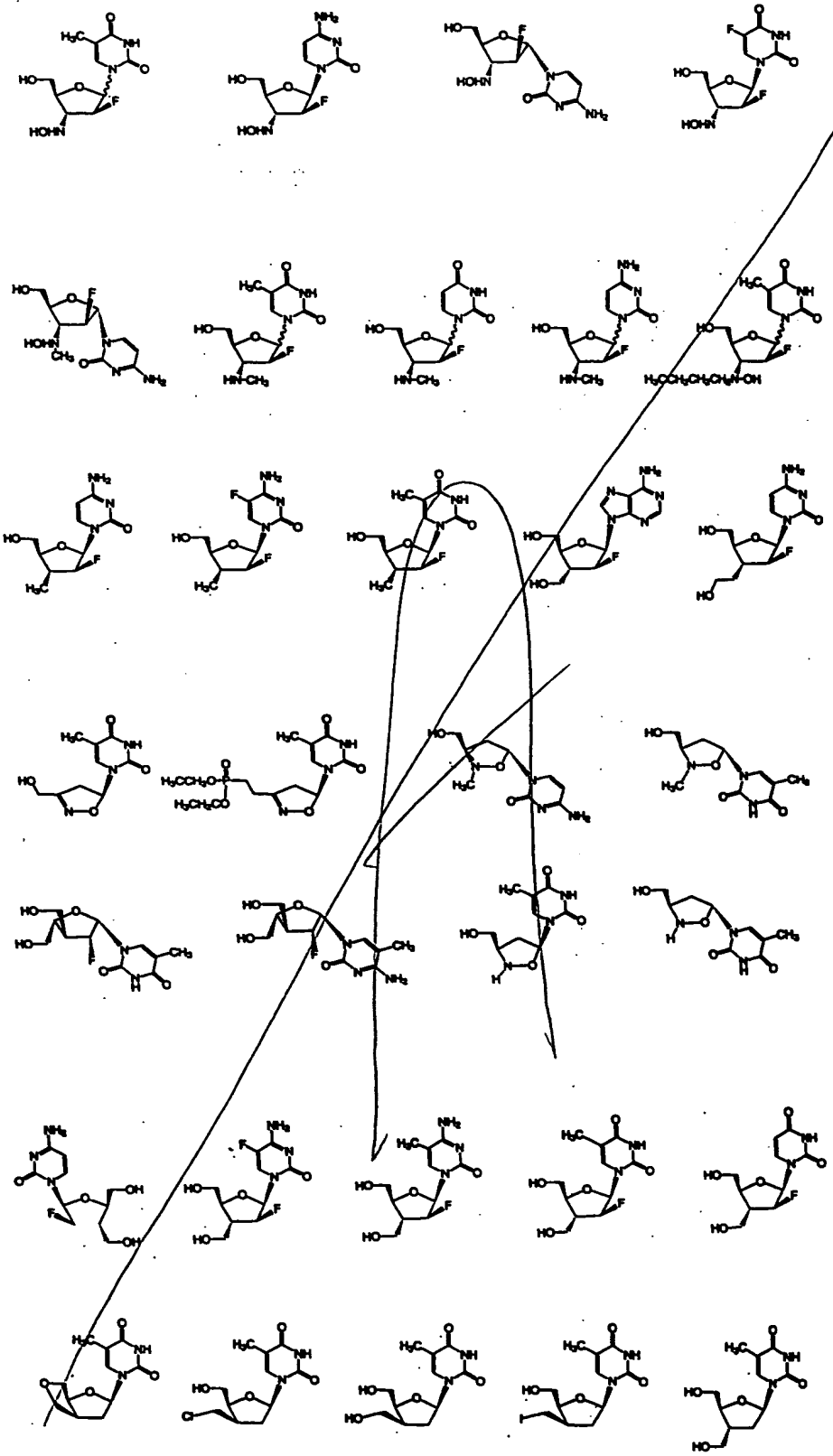


or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

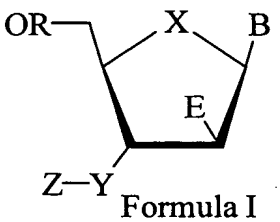
10. The method of Claim 9, further comprising administering the compound in combination or alternation with one or more additional anti-HDV agents.

11. The method of Claim 10, wherein the additional HDV agent is selected from the group consisting of FTC (the (-)-enantiomer or the racemate), L-FMAU, interferon, beta-D-dioxolanyl-guanine (DXG), beta-D-dioxolanyl-2,6-diaminopurine (DAPD), beta-D-dioxolanyl-6-chloropurine (ACP), beta-D-dioxolanyl-2-aminopurine (ADP), famciclovir, penciclovir, bis-POM PMEA (adefovir dipivoxil); lobucavir, ganciclovir, ribavarin, lamivudine (3TC), L-thymidine (L-dT), L-2'-deoxycytidine (L-dT), L-2'-deoxycytidine-3',5'-di-O-valyl (D or L), entecavir (BMS-200475), adefovir, L-D4FC, D-D4FC, and mycophenolic acid (an IMPDH inhibitor).

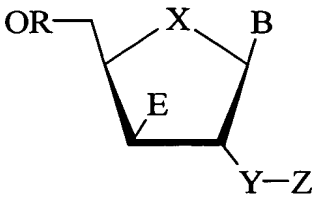
12. The method of Claim 9, wherein the compound is selected from the group consisting of



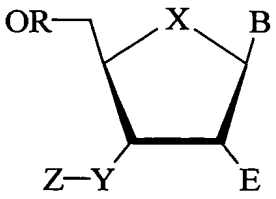
13. A method for the treatment of HIV or AIDS comprising administering an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



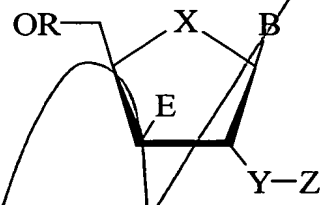
Formula I



Formula III



Formula II



Formula IV

wherein:

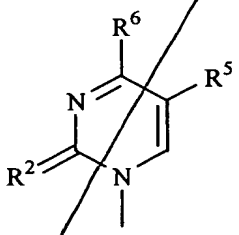
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

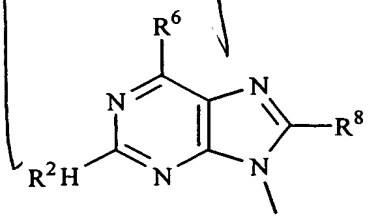
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



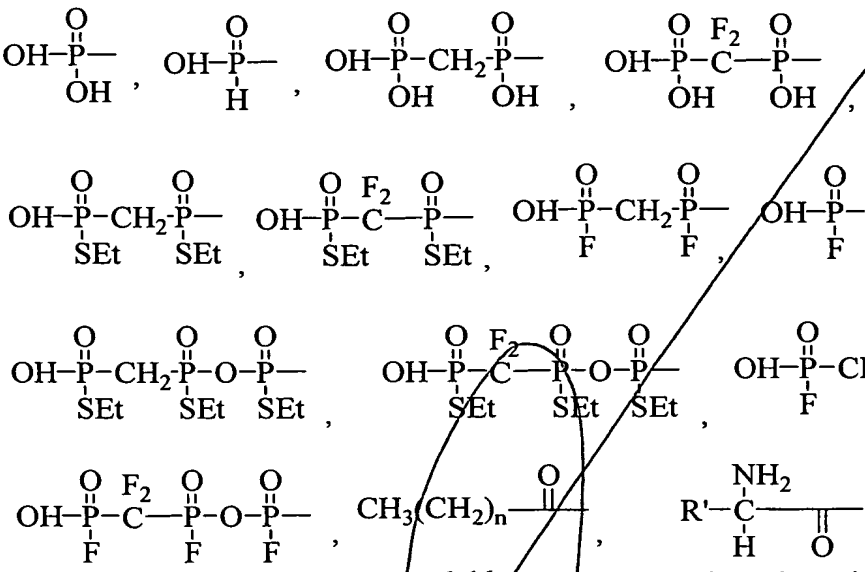


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, CH=CH_2, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of



n=1-16

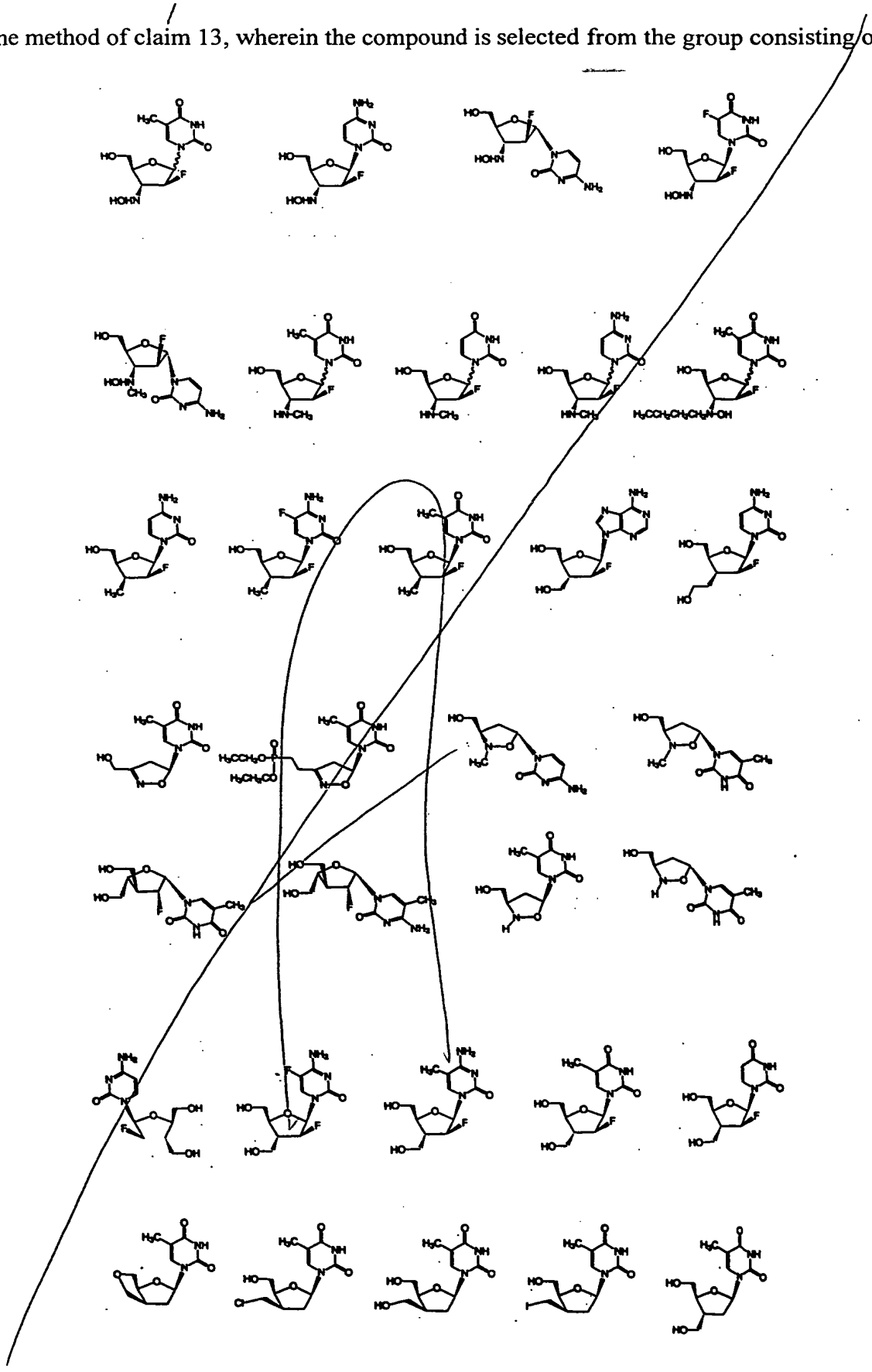
(D- and L-aminoacyl)

or a pharmaceutically acceptable salt or prodrug thereof, optionally in combination with a pharmaceutically acceptable carrier.

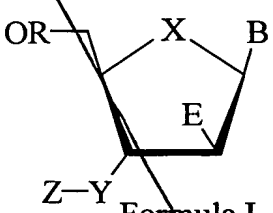
14. The method of Claim 13, further comprising administering the compound in combination or alternation with one or more additional anti-HIV agents.

15. The method of Claim 14, wherein the additional anti-HIV agent is selected from the group consisting of (-) or racemic 2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane (FTC); the (-)-enantiomer of 2-hydroxymethyl-5-(cyostin-1-yl)-1,3-oxathiolane (3TC); carbovir, acyclovir, interferon, AZT, DDI, DDC, D4T, 3'-azido-2',3-dideoxy-5-methyl-cytidine, beta-D-dioxolanyl-guanine (DXG), beta-D-dioxolanyl-6-chloropurine (ACP), abacavir, SUSTIVA, nevirapine, delavirdine, TMC-120, DMP-266, Loviride, Capravarine, 6-benzyl-1-(ethoxymethyl)-5-isopropyl uracil (MKC-442), indinavir, inverase, viracept, norvir, fortovase, agenerase, lopinavir and DMP-450.

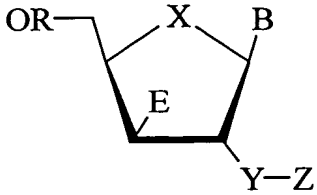
16. The method of claim 13, wherein the compound is selected from the group consisting of



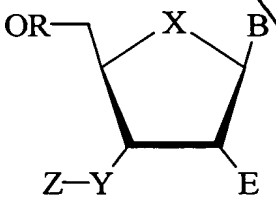
17. A pharmaceutical composition for the treatment of HBV comprising a combination of an effective amount of an anti-HBV agent and an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



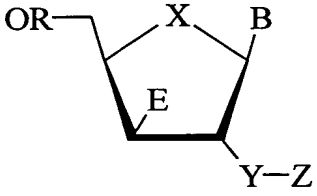
Formula I



Formula III



Formula II



Formula IV

wherein:

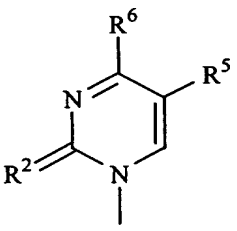
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

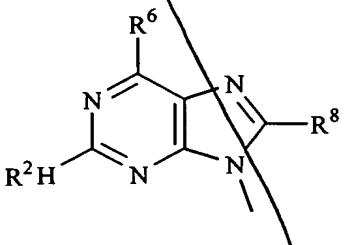
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



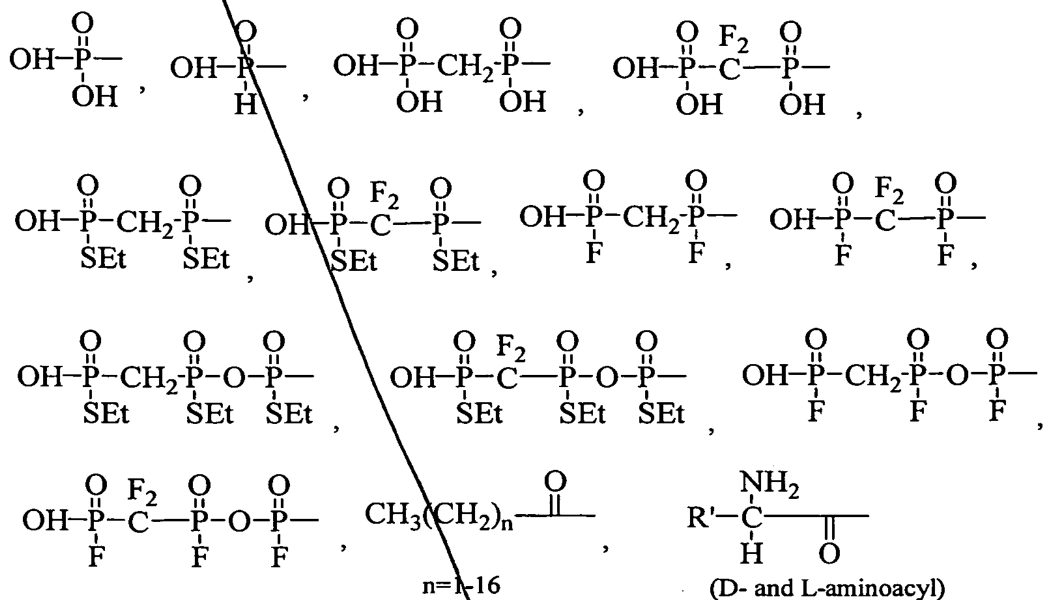


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH=CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

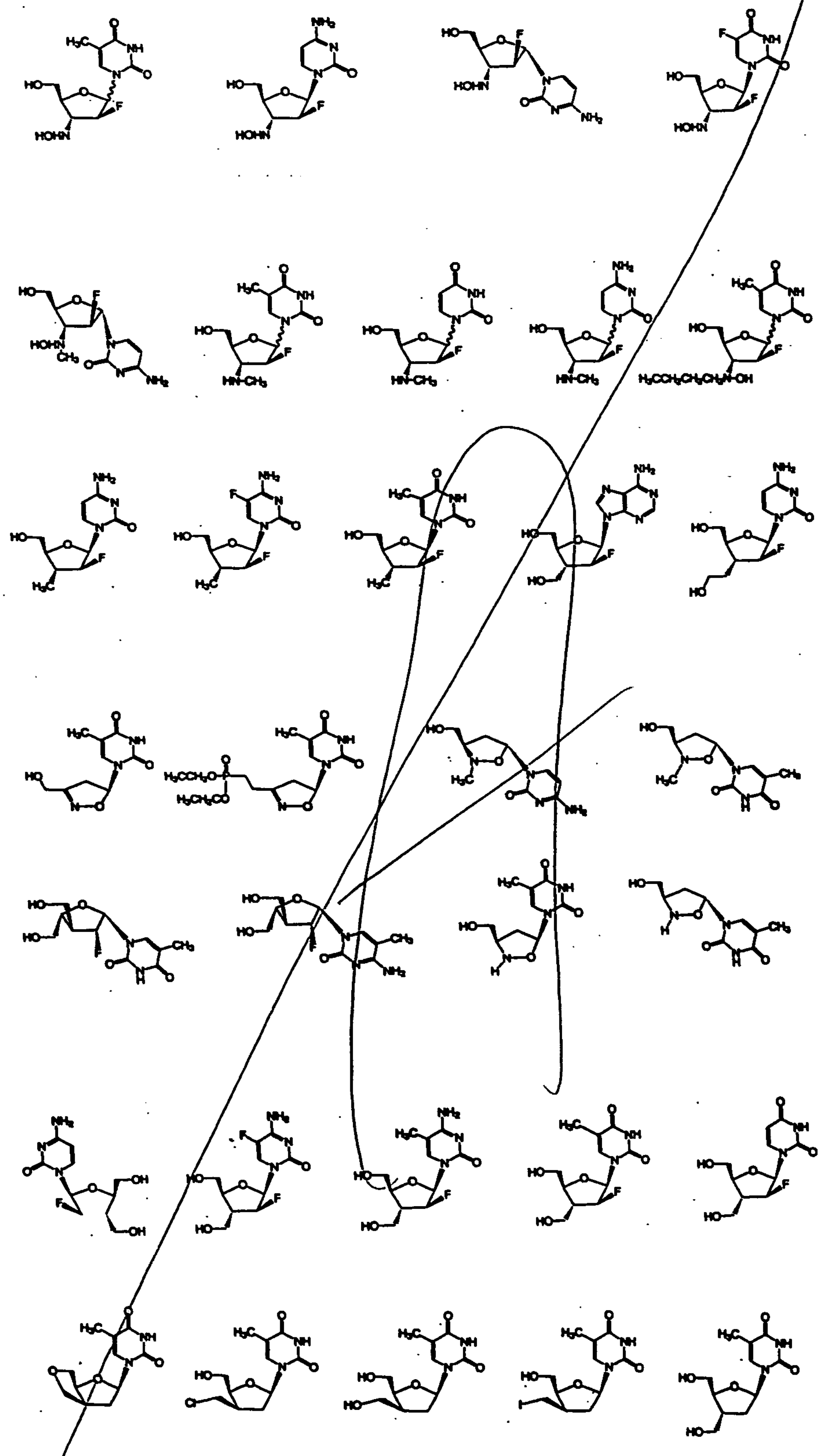
R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of

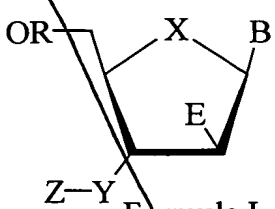


or a pharmaceutically acceptable salt or prodrug thereof, in combination with a pharmaceutically acceptable carrier.

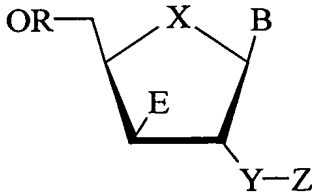
18. The composition of Claim 17, wherein the compound is selected from the group consisting of



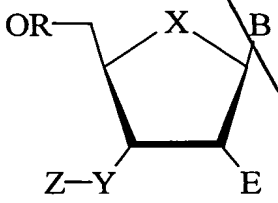
19. A pharmaceutical composition for the treatment of HCV comprising an anti-HCV agent and an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



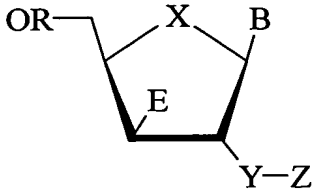
Formula I



Formula III



Formula II



Formula IV

wherein:

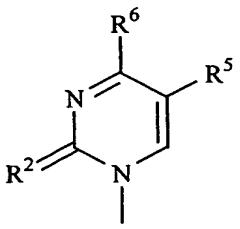
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

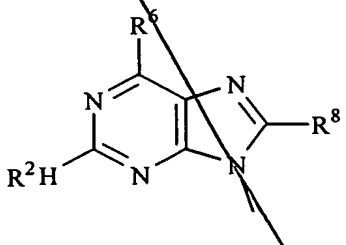
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



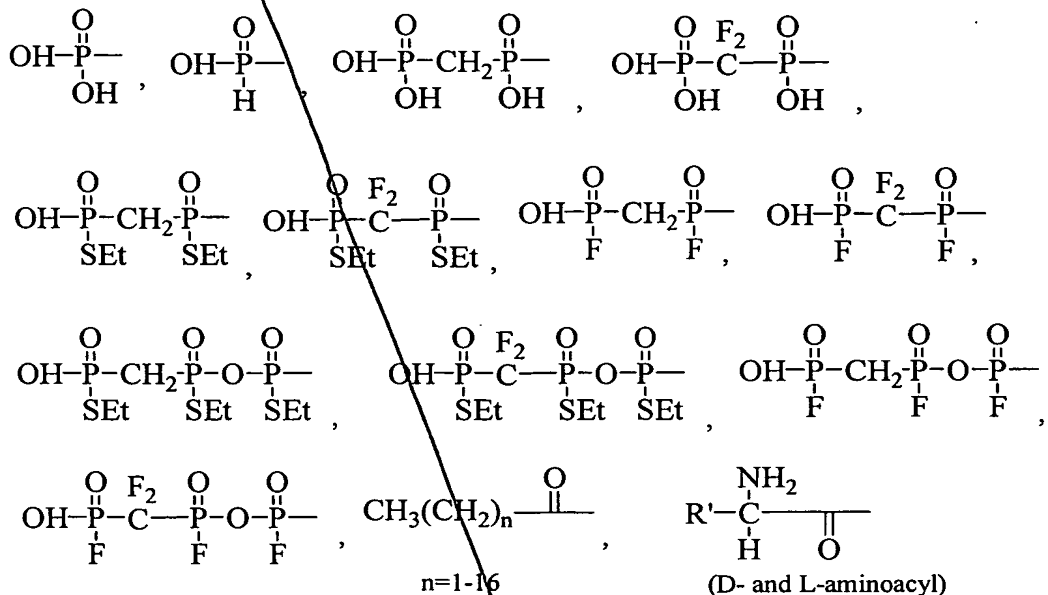


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH{=}CH_2$, $CH{=}CHBr$, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

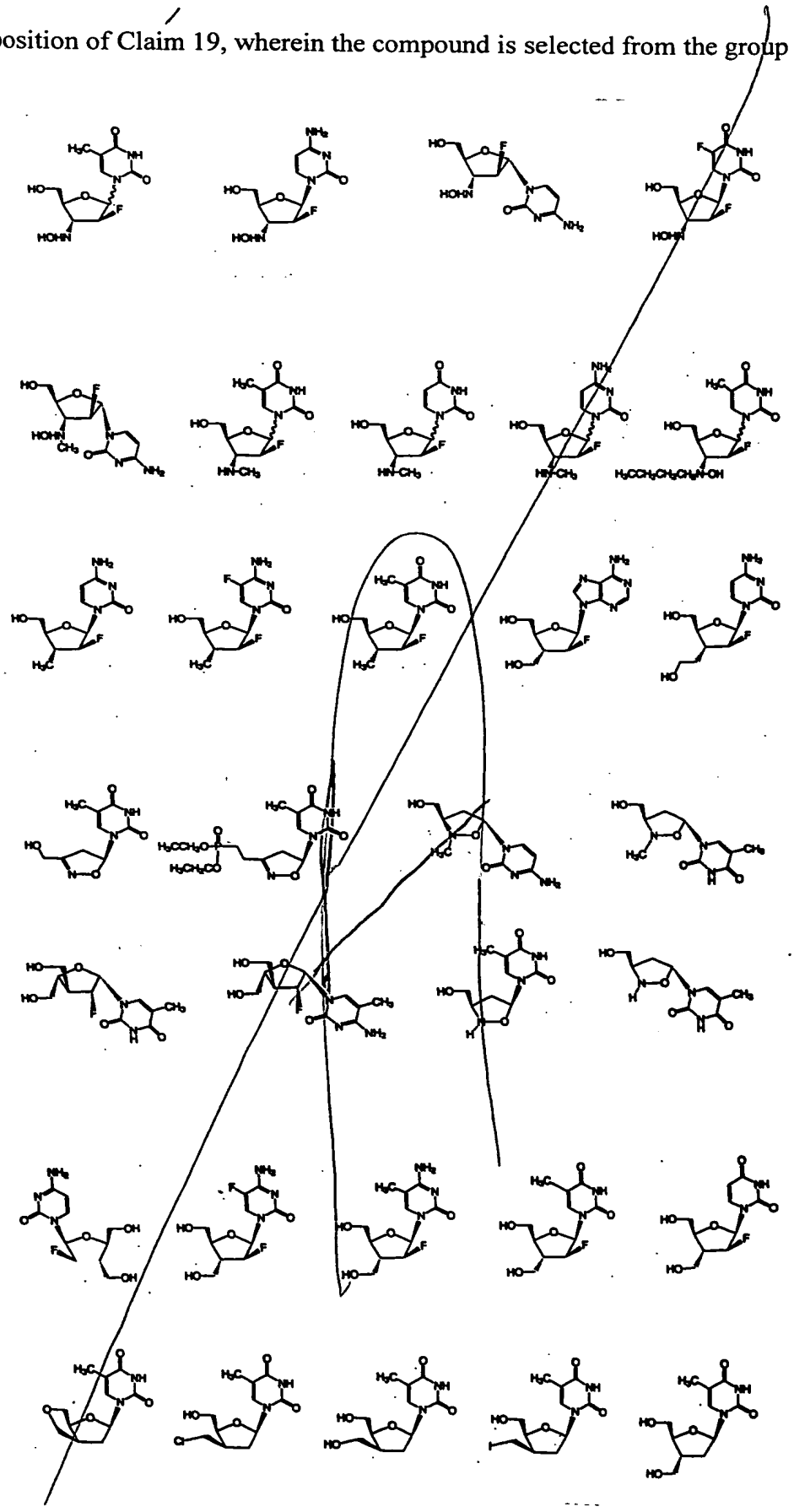
R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of

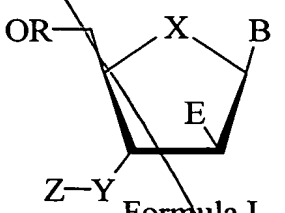


or a pharmaceutically acceptable salt or prodrug thereof, in combination with a pharmaceutically acceptable carrier.

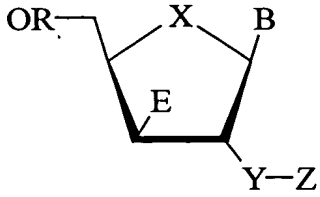
20. The composition of Claim 19, wherein the compound is selected from the group consisting of



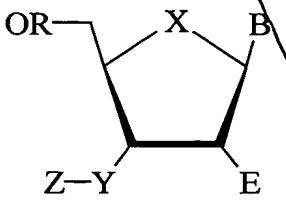
21. A pharmaceutical composition for the treatment of HDV comprising an anti-HDV agent and an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



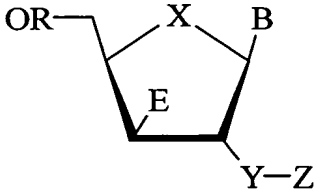
Formula I



Formula III



Formula II



Formula IV

wherein:

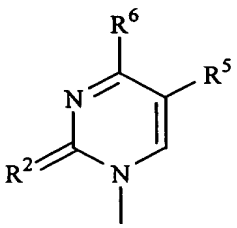
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

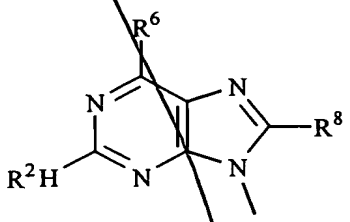
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



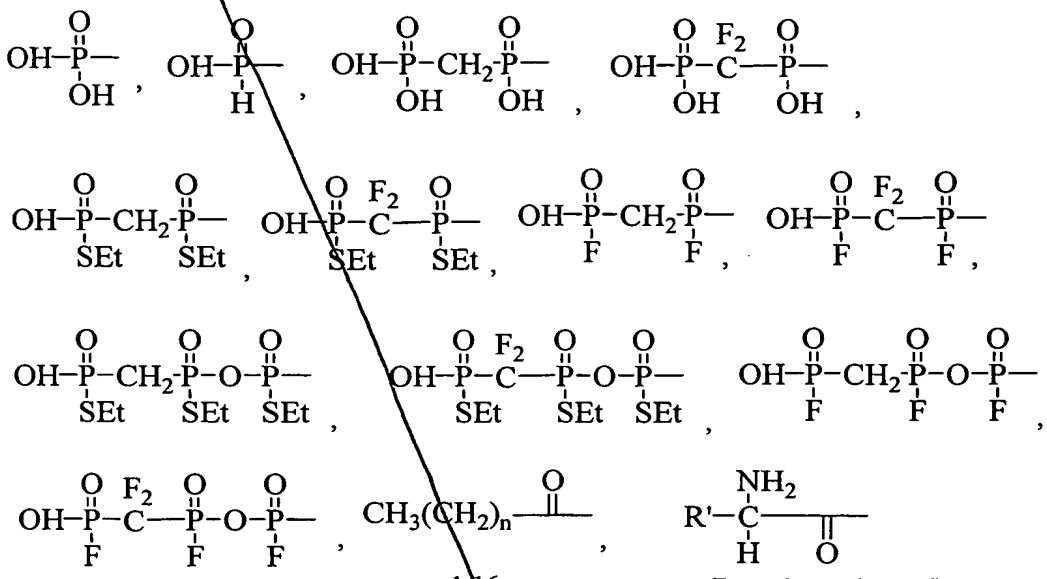


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH{=}CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

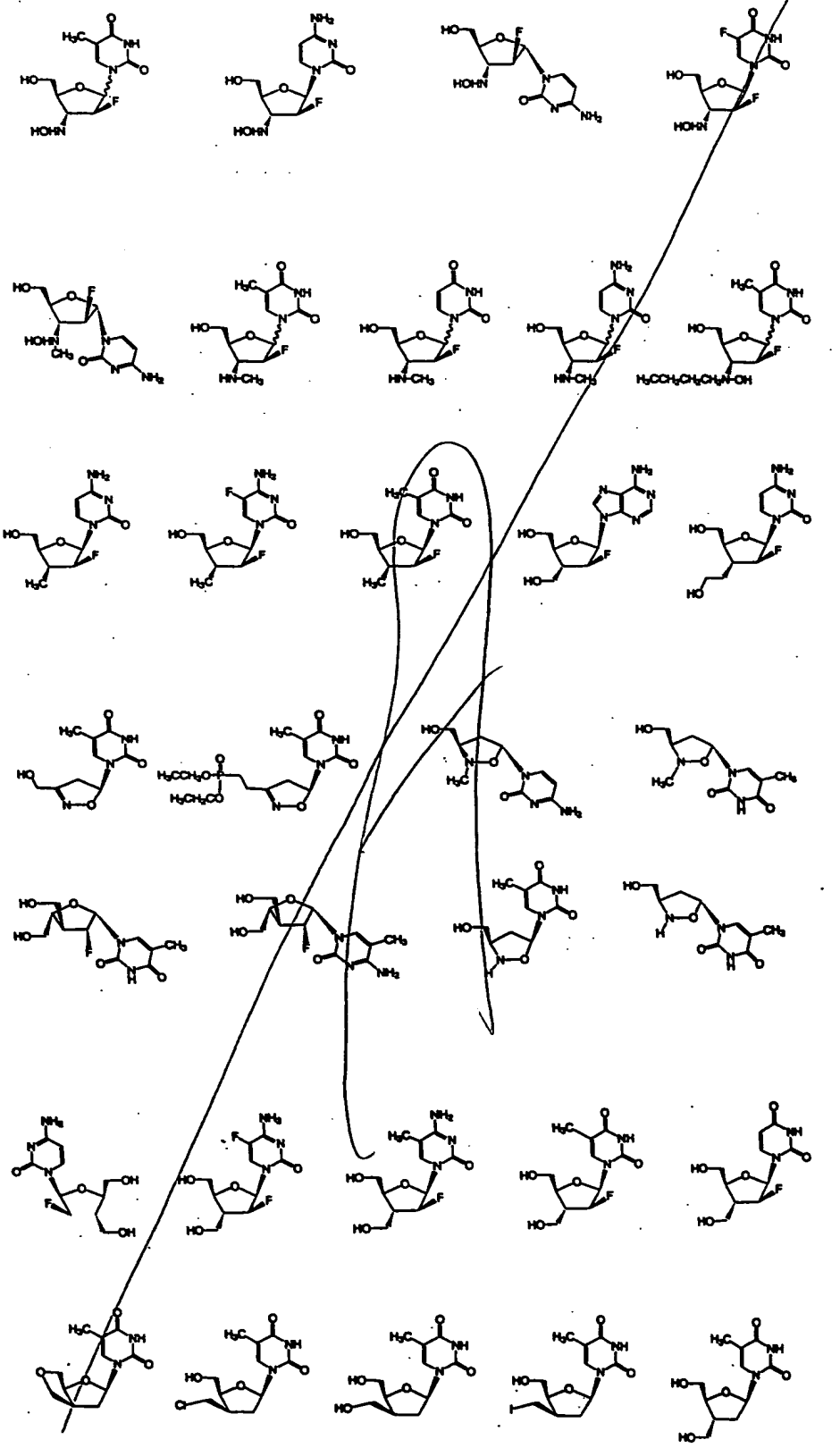
R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

R is independently selected from the group consisting of

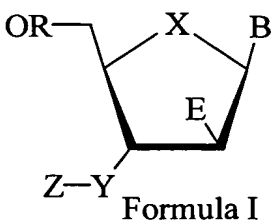


or a pharmaceutically acceptable salt or prodrug thereof, in combination with a pharmaceutically acceptable carrier.

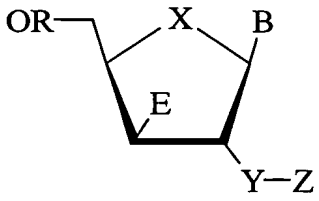
22. The composition of claim 21, wherein the compound is selected from the group consisting of



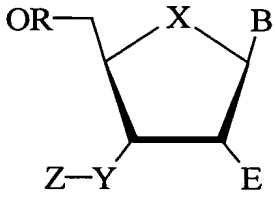
23. A method for the treatment of a proliferative disorder comprising administering an effective amount of a compound selected from the group consisting of formulas [I]-[IV] below and mixtures of two or more thereof:



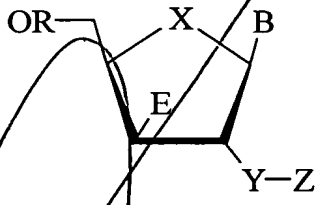
Formula I



Formula III



Formula II



Formula IV

wherein:

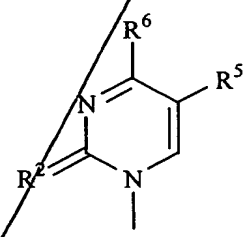
E is selected from the group consisting of H, OH, OMe, SH, SMe, NH_2, NHMe, N_3, F, Cl, Br, CO_2H, CO_2-alkyl, OPh, $OPhNO_2$, NO, NO_2, SCN, OCN, NCS, NCO, SOMe, SO_2Me;

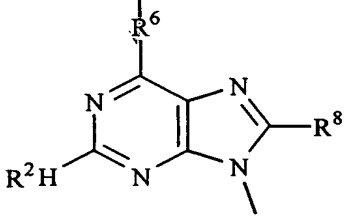
X is selected from the group consisting of O, S, NH, CH_2, CHF, CF_2;

Y is selected from the group consisting of CH_2, NH, NOH, NMe, NEt, NOMe, CHF, CF_2;

Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe;

B is a base selected from the group consisting of



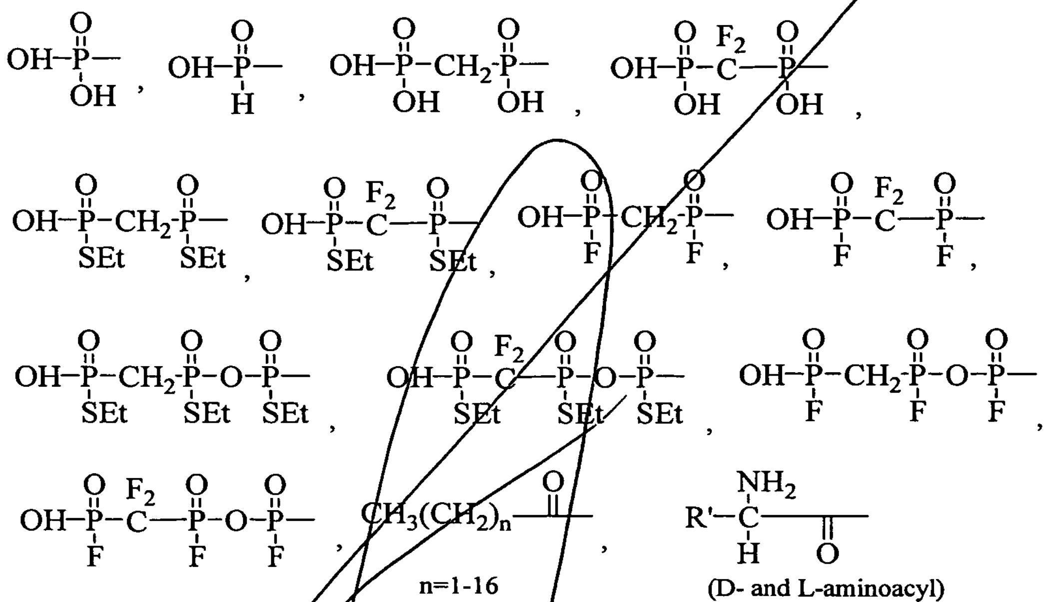


R^2 is selected from the group consisting of O, S, NH, NR;

R^5 is selected from the group consisting of H, branched or unbranched lower alkyl having from 1-5 carbon atoms, F, Cl, Br, I, $CH{=}CH_2$, CH=CHBr, Ph, Ac, OMe, OPh, NO, NO_2, NH_2, NHR;

R^6 and R^8 are the same or different and are independently selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH_2, NHMe, NMe_2;

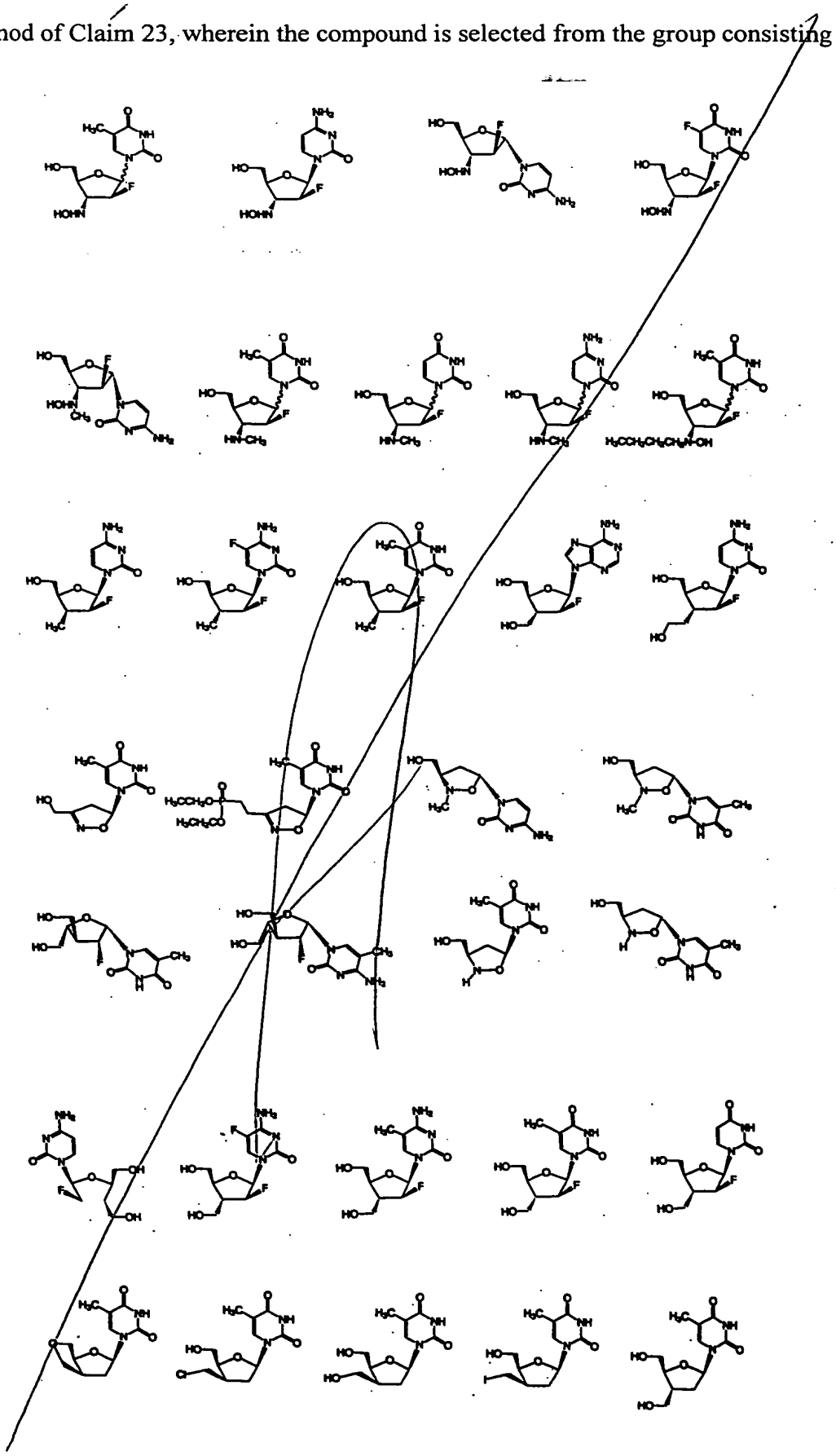
R is independently selected from the group consisting of



or a pharmaceutically acceptable salt or prodrug thereof, in combination with a pharmaceutically acceptable carrier.

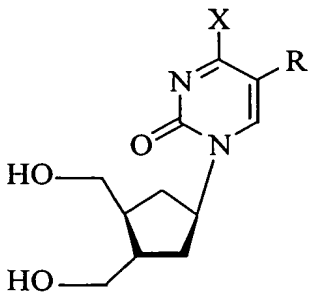
24. The method of Claim 23, wherein the proliferative disorder is selected from the group consisting of cancer of the stomach, kidney, colon, rectal, liver, pancreatic, lung, breast, cervix uteri, corpus uteri, ovary, prostate, testis, bladder, renal, brain/CNS, head and neck, throat, Hodgkin's disease, non-Hodgkin's leukemia, multiple myeloma leukemias, skin melanoma, acute lymphocytic leukemia, acute myelogenous leukemia, small cell lung cancer, choriocarcinoma, rhabdomyosarcoma, neuroblastoma, mouth/pharynx, esophagus, larynx, melanoma, and lymphoma.

25. The method of Claim 23, wherein the compound is selected from the group consisting of



26. A process for stereospecifically preparing a 5'-modified pyrimidine β-nucleoside comprising

a. applying the Mitsunobu reaction to a chiral compound of the formula



b. selectively protecting the 3'-β-position of the resulting nucleoside of step (a) with a benzoyl protecting group or an acid labile protecting group;

c. subjecting the resulting 3'-β-protected anhydro derivative of step (b) to mild alkaline hydrolysis, followed by phosphorylating the ring-opened, 3'-β-protected product with a phosphorylating agent;

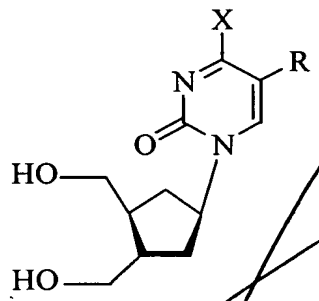
d. saponifiction of the benzoyl group of the resulting product of step (c) to give the desired β-nucleoside 5'-phosphate; and

e. optionally oxidizing the 5'-phosphate to obtain the 5'-phosphite.

27. The process of Claim 26, wherein the acid labile agent is selected from the group consisting of tetrahydropyranyl (THP), a trityl group, or dimethyl-*t*-butylsilyl (DBMS).

28. A process for stereospecifically preparing 5'-phosphorylated pyrimidine α-nucleosides comprising

a. applying the Mitsunobu reaction to a chiral compound of the formula

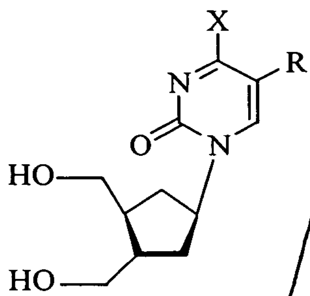


b. directly phosphorylating the resulting anhydro-derivative of step (a) to yield the α-nucleoside 5'-phosphate; and

c. optionally oxidizing the resulting 5'-phosphate to obtain the 5'-phosphite.

29. A process for stereospecifically preparing 5'-phosphorylated pyrimidine α-nucleosides comprising

a. treating a compound of the formula



with CBr_4-Ph_3P to yield a dibromide;

b. treating the dibromide with a non-nucleophilic base in an inert solvent to form an anhydro-nucleoside; and

c. treating the anhydro-nucleoside with tribenzylphosphite, followed by hydrogenation to yield the α-nucleoside 5'-phosphorylated product.

30. A process for preparing purine β-nucleoside 5'-phosphates comprising

a. converting a purine nucleoside into an 8-thio-derivative by brominating the nucleoside and then treating with thiourea;

b. applying the Mitsunobu reaction to the 8-thio-derivative to yield the S-anhydro product having a β-3'-hydroxy group;

c. protecting the β-3'-hydroxy group with a base stable protecting group yielding a protected S-anhydro-nucleoside;

d. oxidizing the protected S-anhydro-nucleoside with m-chloroperbenzoic acid;

e. achieving Pummerer rearrangement of the product of step (d) using benzoic anhydride;

f. desulfurizing the product of step (e) with Raney nickel, followed by de-O-benzoylation in base to yield the protected β-3'-nucleoside;

g. phosphorylating the protected β-3'-nucleoside to obtain the β-5'-phosphorylated product; and

h. optionally oxidizing the product of step (g) to obtain the β-5'-phosphite nucleoside.

31. A process for preparing purine α-nucleoside 5'-phosphates comprising

a. converting a purine nucleoside into an 8-thio-derivative by brominating the nucleoside and then treating with thiourea;

b. applying the Mitsunobu reaction to the 8-thio-derivative to yield an S-anhydro nucleoside product;

c. phosphorylating the S-anhydro nucleoside to yield a protected S-anhydro nucleoside;

d. oxidizing the protected S-anhydro-nucleoside with m-chloroperbenzoic acid;

e. achieving Pummerer rearrangement of the product of step (d) using benzoic anhydride;

f. desulfurizing the product of step (e) with Raney nickel, followed by de-O-benzoylation in base to yield a phosphorylated β-3'-nucleoside;

g. optionally oxidizing the product of step (f) to obtain the β-3'-phosphite nucleoside.

32. A process for preparing nucleoside 5'-di- and triphosphates comprising

a. addition of sulfur to methylenediphosphite tetrachloride to produce di- or trithiomethylenebis(phosphonate) tetrachloride;

b. hydrolyzing the di- or trithiomethylenebis(phosphonate) tetrachloride to obtain the corresponding phosphonate;

c. treating the resulting compound of step (b) under Yoshikawa-Roeschler's conditions to yield the corresponding P^1-nucleoside-5'-yl-methylenebis-(thiophosphonate);

d. S-alkylating and treating the resulting compound of step (c) with fluoride (Bu_4NF, DAST) to yield fluorine substituted 3'-β-protected nucleoside;

e. deprotecting the 3'-β-nucleoside to obtain the 5'-di- or 5'-triphosphate β-nucleoside.

add A7